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=> s (CPT-11 or irinotecan or camptostar)
L1       10060 (CPT-11 OR IRINOTECAN OR CAMPTOSTAR)

=> s (TRAIL or DR5 or Apo2)
L2       20664 (TRAIL OR DR5 OR APO2)

=> s l1 and l2
L3          34 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4           17 DUP REM L3 (17 DUPLICATES REMOVED)

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   2 FILES SEARCHED...
   4 FILES SEARCHED...
L5           4 L4 AND PY<=1999

=> d ibib abs 1-4

L5   ANSWER 1 OF 4     MEDLINE
ACCESSION NUMBER:    2000090232     MEDLINE
DOCUMENT NUMBER:     20090232   PubMed ID: 10626806
TITLE:               Tumor necrosis factor-related apoptosis-inducing ligand's
                     antitumor activity in vivo is enhanced by the
                     chemotherapeutic agent CPT-11.
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AUTHOR: Gliniak B; Le T
CORPORATE SOURCE: Department of Molecular Immunology, Immunex Corp., Seattle, Washington 98101, USA.. gliniak@immunex.com
SOURCE: CANCER RESEARCH, **(1999 Dec 15)** 59 (24) 6153-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB Tumor necrosis factor-related apoptosis-inducing ligand (**TRAIL**) can induce apoptosis in a wide variety of transformed human cells in vitro. In this study, the antitumor activity of recombinant **TRAIL** was analyzed in mice bearing human colon carcinoma tumors. We found that these tumors displayed a differential sensitivity to **TRAIL** in vivo that paralleled their susceptibility to **TRAIL**-induced apoptosis in vitro. Treatment of **TRAIL**-sensitive tumors 3 days after tumor challenge resulted in a dose-dependent inhibition of growth and the elimination of tumors in many mice. Colon carcinoma cell lines could be further sensitized to **TRAIL**-induced apoptosis in vitro by the addition of the chemotherapeutic agent camptothecin. Moreover, the combination of **TRAIL** and **CPT-11**, a water-soluble analogue of camptothecin, greatly enhanced the antitumor activity of **TRAIL** in vivo. **TRAIL** plus **CPT-11** treatment of both 3- and 10-day established **TRAIL**-sensitive tumors resulted in both a significant inhibition of tumor growth and a high proportion of complete tumor regressions. Treatment of **TRAIL**-resistant tumors with **TRAIL** and **CPT-11** dramatically slowed tumor growth and induced a transient tumor regression. These data demonstrate that **TRAIL** alone is a potent antitumor agent in vivo, and its activity can be significantly enhanced in combination with the chemotherapeutic agent **CPT-11**.

L5 ANSWER 2 OF 4 MEDLINE
ACCESSION NUMBER: 1999340100 MEDLINE
DOCUMENT NUMBER: 99340100 PubMed ID: 10411544
TITLE: Safety and antitumor activity of recombinant soluble **Apo2** ligand.
AUTHOR: Ashkenazi A; Pai R C; Fong S; Leung S; Lawrence D A; Marsters S A; Blackie C; Chang L; McMurtrey A E; Hebert A; DeForge L; Koumenis I L; Lewis D; Harris L; Bussiere J; Koeppen H; Shahrokh Z; Schwall R H
CORPORATE SOURCE: Department of Molecular Oncology, Genentech Inc., 1 DNA Way, South San Francisco, CA 94080-4990, USA.
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, **(1999 Jul)** 104 (2) 155-62.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 19990820
Entered Medline: 19990812

AB TNF and Fas ligand induce apoptosis in tumor cells; however, their severe toxicity toward normal tissues hampers their application to cancer therapy. **Apo2** ligand (Apo2L, or **TRAIL**) is a related molecule that triggers tumor cell apoptosis. Apo2L mRNA is expressed in many tissues, suggesting that the ligand may be nontoxic to normal cells. To investigate Apo2L's therapeutic potential, we generated in bacteria a

potently active soluble version of the native human protein. Several normal cell types were resistant in vitro to apoptosis induction by Apo2L. Repeated intravenous injections of Apo2L in nonhuman primates did not cause detectable toxicity to tissues and organs examined. Apo2L exerted cytostatic or cytotoxic effects in vitro on 32 of 39 cell lines from colon, lung, breast, kidney, brain, and skin cancer. Treatment of athymic mice with Apo2L shortly after tumor xenograft injection markedly reduced tumor incidence. Apo2L treatment of mice bearing solid tumors induced tumor cell apoptosis, suppressed tumor progression, and improved survival. Apo2L cooperated synergistically with the chemotherapeutic drugs 5-fluorouracil or **CPT-11**, causing substantial tumor regression or complete tumor ablation. Thus, Apo2L may have potent anticancer activity without significant toxicity toward normal tissues.

L5 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1994:486525 BIOSIS
DOCUMENT NUMBER: PREV199497499525
TITLE: 7-Ethyl-10-(4-(1-piperidino)-1-piperidino) carbonyloxy camptothecin: Mechanism of resistance and clinical **trails**.
AUTHOR(S): Saijo, Nagahiro (1); Nishio, Kazuto; Kubata, Naohiro; Kanzawa, Fumihiko; Shinkai, Tetsu; Karato, Atsuya; Sasaki, Yasutsuna; Eguchi, Kenji; Tamura, Tomohide; et al.
CORPORATE SOURCE: (1) Pharmacol. Div., Natl. Cancer Cent. Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104 Japan
SOURCE: Cancer Chemotherapy and Pharmacology, (1994) Vol. 34, No. SUPPL., pp. S112-S117.
ISSN: 0344-5704.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The camptothecin derivative 7-ethyl-10-(4-(1-piperidino)-1-piperidino)-carbonyloxy camptothecin (**CPT-11**) has attracted the attention of clinicians because of its high antitumor activity against refractory solid cancers. We established two **CPT-11**-resistant cell lines, a non-small-cell lung-cancer cell line (PC-7/**CPT-11**) from the parental PC-7 line and an ovarian cancer cell line (HAC-2/**CPT-11**) from the parental HAC-2 line. The mechanisms of resistance to **CPT-11** in PC-7/**CPT-11** cells were reduced conversion of **CPT-11** to its active metabolite SN-38 and point mutation of topoisomerase I. Those in HAC-2/**CPT-11** cells were reduction of topoisomerase I activity and decreased sensitivity of topoisomerase to topoisomerase I inhibitors. No point mutation of the topoisomerase was observed in HAC-2/**CPT-11** cells. We conducted two phase I trials using **CPT-11** in combination with other anticancer agents. One was a phase I trial of **CPT-11** and cisplatin given with a fixed dose of vindesine to patients with advanced non-small-cell lung-cancer and the other was a phase I study on a topoisomerase-targeting combination of **CPT-11** and etoposide (VP-16) in patients with various malignant solid tumors. The results of the first trial indicated that the recommended dose of **CPT-11** for phase II studies was 80 mg/m-2 combined with 3 mg/m-2 vindesine on days 1 and 8 and 60 mg/m-2 cisplatin on day 1. In the second trial, the recommended dose of **CPT-11**/VP-16 given with recombinant granulocyte colony-stimulating factor (on days 4-17) was found to be 60/60 mg/m-2. In both trials, diarrhea and granulocytopenia were considered to be dose-limiting toxicities.

L5 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999247940 EMBASE
TITLE: Prognostic factors of non-small cell lung cancer patients with malignant pleural effusion.
AUTHOR: Seto T.; Semba H.; Seto M.; Nishida Y.; Fukai Y.

CORPORATE SOURCE: T. Seto, Division of Respiratory Diseases, Kumamoto Regional Medical Center, Kumamoto, Japan
SOURCE: Japanese Journal of Lung Cancer, (1999) 39/3 (303-308).
Refs: 12
ISSN: 0386-9628 CODEN: HGANAO
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB Prognostic factors in 70 patients with non-small cell lung cancer (NSCLC) with malignant pleural effusion at initial treatment were examined retrospectively. They constituted 11% of the patients with NSCLC, diagnosed at our hospital from 1990 to 1997. Although 9 of the patients had negative in effusion cytology findings, malignant effusion was diagnosed by thoracoscopic pleural biopsy under local anesthesia. Of the patients with malignant pleural effusion 89% were adenocarcinoma of the lung. Using non-parametorical method analyses, N-factor (p=0.0105), clinical stage (0.0247), ECOG performance status (0.001), protein value of effusion (0.0095), and effusion volume/day (0.0019) were recognized as prognostic factors. Furthermore, N-factor and low protein value of effusion were poor predictive factors for survival, and intra-pleural chemotherapy and systemic chemotherapy were related to good survival in multivariate analysis. In clinical **trail** for patients with malignant pleural effusion, we must carefully compare these pre-treatment factors.

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NEWS  4  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
NEWS  5  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS  6  Aug 26  Sequence searching in REGISTRY enhanced
NEWS  7  Sep 03  JAPIO has been reloaded and enhanced
NEWS  8  Sep 16  Experimental properties added to the REGISTRY file
NEWS  9  Sep 16  CA Section Thesaurus available in CAPLUS and CA
NEWS 10  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11  Oct 24  BEILSTEIN adds new search fields
NEWS 12  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
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NEWS 15  Dec 04  CSA files on STN
NEWS 16  Dec 17  PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17  Dec 17  TOXCENTER enhanced with additional content
NEWS 18  Dec 17  Adis Clinical Trials Insight now available on STN
NEWS 19  Jan 29  Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
NEWS 20  Feb 13  CANCERLIT is no longer being updated
NEWS 21  Feb 24  METADEX enhancements
NEWS 22  Feb 24  PCTGEN now available on STN
NEWS 23  Feb 24  TEMA now available on STN
NEWS 24  Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 25  Feb 26  PCTFULL now contains images
NEWS 26  Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27  Mar 19  APOLLIT offering free connect time in April 2003
NEWS 28  Mar 20  EVENTLINE will be removed from STN
NEWS 29  Mar 24  PATDPAFULL now available on STN
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NEWS 31  Apr 11  Display formats in DGENE enhanced
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NEWS 33  Apr 17  Polymer searching in REGISTRY enhanced
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NEWS 35  Apr 21  New current-awareness alert (SDI) frequency in
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NEWS 36  Apr 28  RDISCLOSURE now available on STN
NEWS 37  May 05  Pharmacokinetic information and systematic chemical names
                 added to PHAR

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              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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